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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/479,995	06/07/95	[illegible]	[illegible]

EXAMINER	
ART UNIT	PAPER NUMBER
1809	

DATE MAILED: [illegible]

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Application No.	Applicant(s)	
08/479,995	Pergolizzi et al.	
Examiner	Group Art Unit	
Ardin Marschel	1809	

Office Action Summary

☒ Responsive to communication(s) filed on 6-7-95, 3-5-96, 4-12-96, and 4-15-96

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 283-438 is/are pending in the application.

~~Of the above~~, Claim(s) 1-282 have been canceled. ~~is/are withdrawn from consideration~~.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 283-438 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

Notice of References Cited, PTO-892

Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☑ Notice of Draftsperson's Patent Drawing Review, PTO-948

Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

The art unit designated for this application has changed. Applicant(s) are hereby informed that future correspondence should be directed to Art Unit 1809.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as the specification, as originally filed, does not provide support for the invention as is now claimed.

In claim 300, lines 3-4, the phrase "an analog-containing polymer" which adds NEW MATTER in that written basis for generic polymers containing analogs has not been found. Consideration of the support cited by applicants reveals that polynucleotides of various types are listed but not more generic polymers. Another interpretation is that NEW MATTER is added via unclarity of the metes and bounds of such polymers. Claims 315, 321, and 328 also contain this NEW MATTER and claims 317 and 318 via dependence from the above claims.

In claim 313, line 2, the phrase "partially double-stranded" is given. Consideration of the written support as filed has failed to reveal any written basis for "partially" double-stranded. This "partially" is thereofore NEW MATTER. Claims 319 and 331 also contain this NEW MATTER.

Claims 365, 383, 401, and 407 are directed to a specific order of complex formation wherein the bridging entity is first contacted with the signalling entity to form a first complex followed by contacting this first complex with the analyte. Consideration of the support cited by applicants on pages 33-34 has not revealed a written basis for this order of complex formation. Therefore the limitations in claims 365, 383, 401, and 407 directed to the above summarized order lack written basis as filed and contain NEW MATTER and claims 404 and 410 via dependence from the above claims.

Claim 300, 313, 315, 317-319, 321, 328, 331, 365, 383, 401, 404, 407, and 410 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the above objections to the specification.

Claims 283-438 are rejected, as discussed below, under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 287, line 2, "more than one molecular bridging entity" is cited. In lines 7-8, "said bridging entity" is cited. This citation in lines 7-8 lacks antecedent basis because it directs this portion of the second part of the claimed composition to "said bridging entity" as a single item. Confusingly, there is no such "single" bridging entity described previously in the claim. Instead line 2 cites multiple bridging entities via the phrase "more than one". It is unclear which

bridging entity is intended in lines 7-8 out of the multiple bridging entities cited in line 2. Lines 7-8 suggest that there is some particular bridging entity that is being referred to. Since there are only multiple bridging entities in line 2, the is no antecedent basis for the liness 7-8 citation of a particular or single bridging entity. Claims 288-290 also contain this unclarity as well as claims dependent therefrom. Clarification of this via clearer claim wording is requested.

Claims 283 etc. cites "a first part" and "a second part" wherein each "part" contains portions wherein the relationship(s) between these portions are undefined in the claims. See the below specific claim 291 explanation as an example of the unclarity in the definition of each "part" as given in the instant claims.

Claim 291, lines 8-9, cite "one or more polynucleotides..." but without defining their relationship to the portion that is capable of binding or hybridizing with the bridging entity. Since line 6 of claim 291 cites "a second part", this is suggestive of part (singular). Such a singular part would be expected to contains portions that are attached, linked, bound together, or related in some way. No such relationship has been defined between the two portions of the "part" of lines 6-9 of claim 291. Do applicants intend that lines 6-9 of claim 291 disclose a singular part or, alternatively, a part made up of portions which are not required to be attached or related in some way? A "part" made up of unrelated portions is vague and

indefinite because this is interpretable as "parts" but is confusingly not cited in the claim as "parts". Another unclarity is that line 6 cites the second part as comprising "more than one signalling entity", each such entity comprising...", but confusingly lacks any designation of what performs the signalling function thereafter in the claim. Claims 292-294 also contain the above unclarities as well as claims dependent therefrom. Clarification is requested via clearer claim wording.

Claims 300 and 310 are vague and definite beyond the above unclarities in that the respective lines 1 cite "said nucleic acid" without clear antecedent basis. It is noted that several nucleic acids are given in the claims from which claims 300 and 310 depend directly or indirectly such as in the analyte in claim 299 and in the molecular bridging and signalling entities. Clarification of the claim wording is requested as to the antecedent basis

Claim 322 etc. is vague and indefinite beyond the above unclarities in that it is unclear what the metes and bounds of the word "derived" are as cited in line 3 therein. Many other claims cite this word also. If there are no limitations on what may be deleted, replaced, or added; such derivation may result in any other composition whatsoever. If that is so, why cite what is being altered as derived? Clarification of what is intended for such derivation practice is requested.

Claim 356 lacks antecedent basis for a singular "molecular bridging entity" wherein claims 287 etc. cite multiple molecular

bridging entites.

Claims 360-362 contain the above unclarities but also are vague and indefinite as to what is meant in that claims 360-362 and claims 283, 284, 291, and 293 appear to be identical except for what the claimed subject matter is called in their respective first lines. For example, in claim 283 the subject matter is a "composition of matter" whereas in claim 360 the subject matter is an "article of manufacture". What difference is meant thereby? Does claim 360 indicate that a manufacturing process in required to prepare the claimed article whereas manufacturing is not required for preparing the composition of claim 283? If manufacturing is not required, is this suggestive that claim 283 includes products of nature within its scope? Clarification of the metes and bounds of each of these types of claims compared to each other is requested.

Claim 438 is vague and indefinite as to what the metes and bounds are for the phrase "nucleic acid analog". Is this meant to be directed to analogs that are no longer nucleic acids but have some nucleic acid type characteristic(s)? Is this meant to be directed to nucleic acids that are modified as compared to naturally occurring nucleic acids? Aren't modified nucleic acids still nucleic acids? What differentiates nucleic acids from nucleic acid analogs? Similarly, in claim 315, line 4, the phrase "an analog-containing polymer" is cited without defining what it is an analog of. A polymer is still a polymer even if modified, isn't it? What is an analog of a polymer? Similarly,

the term "modified" is given in claim 317, line 2, without defining what modifications are practicable therein. What are the metes and bounds of such modifications? Numerous instant claims contain the above unclarities and are rejected also hereinunder. Clarification is requested.

Claims 364, 365, 382, and 383 cite the phrase "said complex" in their respective last lines. This "said complex" lacks clear antecedent basis because two complexes are cited that may be the antecedent. One complex is the "first complex" in line 3 of claims 364, 365, 382, and 383 and a second complex is given in line 4 of claims 363 and 381 from which claims 364, 365, 382, or 383, respectively, depend. Claim 400 contains a similar unclarity.

Claims 283-438 cite the phrase "nucleic acid sequences or segments" either directly or indirectly via claim dependence. This phrase is vague and indefinite as what difference is intended between "sequences" and "segments". Since these are separately cited in the claims, this indicates that a different meaning is intended for each of these items. It is unclear what this different meaning may be. Clarification is requested.

Claims 367 and 368, lines 1-2 of each, contain the phrase "wherein said detecting step the direct" which is awkwardly worded such that it is unclear what is meant thereby. Claims 369, 371-373, 385-387, and 389-391 also contain similar confusing wording.

Claims 374 and 392 are vague and indefinite due to unclarity

of what is meant by the phrase "and a binding step on an insoluble phase". Is this intended to indicate that a binding step is present only within the detecting step of the process or is this intended to indicate that the binding may occur anywhere in the process? It is noted that claim 65, as filed, as pointed to by applicants indicates that the detecting step per se is only limited to comprise a binding step on an insoluble phase. Clarification is requested.

Claims 343-346 are vague and indefinite because it is unclear what is meant by citing the word "indirectly" twice in the last line of claim 343. Does this indicate that at least two linkages are required between the signalling entity and the actual signal producing entity? or some other indirect procedure? Clarification is requested.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 283-296, 298-301, 304, 307, 309-321, 323-333, 335-340, 347, 350, 353, 358-364, 366, 367, 372-376, 378-382, 384, 385, 392-394, 396-400, 402, 403, 405, 406, 408, 409, and 438 are rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Dunn et al.

Dunn et al. reads on the above listed claims due to its

disclosure of an immobilized target analyte wherein a bridging entity is hybridized thereto followed by washing and then the hybridization of a nick translated radiolabelled signalling entity that is made up of a heterogeneous mixture of radiolabelled fragments produced as a result of the nick translation process. This nick translation process also results in a ratio of signalling entities as being clearly greater than 1 as compared to bridging entities, but is unclear how much greater than 1.

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claims 283-301, 304, 307, 309-340, 343-364, 366, 367, 370-376, 378-382, 384, 385, 388, 390-394, 396-400, 402, 403, 405, 406, 408, 409, 411, 413, 414, 416, 418-438 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Dunn et al.(1977) taken in view of Ward et al.(P/N 4,711,955).

The instant invention is directed to compositions for detecting an analyte via the recognition and binding of a bridging entity to the analyte. The bridging entity contains two portions, one portion that recognizes and binds the analyte and a second portion containing a polynucleotide segment. The polynucleotide segment of the second portion of the bridging entity hybridizes to a signalling entity via a complementary nucleic acid segment in the signalling entity. The signalling entity may be non-radioactively labeled so as to be detectable. The detection of the label indicates the presence of analyte. Kit-like compositions for the practice of the method are also claimed. The specific limitations of certain claims are discussed below as to how they are made obvious by the above combination of references. It is noted that instant claim 283 includes a bridging entity with only one second nucleic acid portion within its scope, but even claims such as instant claim 287 which cites multiple bridging entities lacks limiting these multiple entities as including different types or sequences, thus permitting a solution of identical molecules yet within the scope of claim 287. Also, it is noted that the second part of instant claim 283 gives the signalling part as comprising more than one

signalling entity but without requiring either that they must include non-identical entities or that they must contain entities that bind or hybridize to different segments of the second portion of the bridging entity.

Dunn et al.(1977) disclose a sandwich hybridization technique wherein an RNA construct containing two portions performs as a bridging entity as in the instant invention. The two portions of the RNA construct consist of an analyte recognition and binding portion and a tail as discussed on page 23, bridging paragraph between the first and second columns. The tail is a polynucleotide segment that hybridizes to a radiolabeled signalling entity for detection. The detection of the radiolabel is indicative of analyte detection. This methodology is depicted in Dunn et al.(1977) on page 24 in Figure 1 with detection results shown in Figures 2 etc. in the reference. This reference generically discloses the instant invention at said page 23 citation but lacks the use of a non-radioactively labeled signalling entity. Additionally, the generic scope of practice of the sandwich hybridization technique of Dunn et al.(1977) is suggested in that the page 23 summary of the technique is generic in nature and the system disclosed by Dunn et al.(1977) to illustrate the technique is stated as being a "model system" on page 23, second column, line 9. These disclosures clearly suggest a scope broader than that of detecting viral RNA map transcription sites as given in the experimental examples in the reference and include detection of

other target sites in genomes of organisms such as bacteria etc. It is noted that the radiolabelled signalling entities of Dunn et al.(1977) are prepared via nick translation as is an embodiment of biotin labelling in the below given Ward et al. disclosure.

Ward et al. generically discloses the substitution of biotinylated nucleic acids as a non-radioactive label for radiolabeled nucleic acids in hybridization detection methods. The disclosure of Ward et al. includes several motivations for the substitution of non-radioactive labels such as based on biotin for radiolabels in columns 1-3 in the section entitled "BACKGROUND OF THE INVENTION" and also gives a reasonable expectation of success for this substitution via numerous examples therein.

Thus, it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice the compositions composed of bridging and signalling entities using non-radioactive labels for detection as instantly claimed because Dunn et al.(1977) disclose bridging and signalling entities as instantly claimed with radiolabel mediated detection and Ward et al. disclose both the motivation and reasonable expectation of success for substituting non-radioactive labels such as biotin for radiolabel mediated detection during hybridization procedures resulting therefore in the practice of the instantly claimed invention. It is noted that the labelled signal entities of Dunn et al. are disclosed as a nick translated preparation of molecules but that this is not outside of the

scope of the instantly rejected claims as noted above. The nick translated signalling entities are a heterogeneous mixture of various different fragments produced by the nick translation processing. These fragments hybridize to different segments of the bridging entity within the target sequence thereon due to their heterogeneous fragment nature but yet directed to said target. Since the nick translation process is variable regarding the number of nucleic acid fragments made thereby the process reasonably results in many different ratios regarding hybridized segments in the bridging entity as well as how many signalling entities there are relative to the bridging entities thus suggesting a wide range of ratios as given in a number of the instant claims between different parts of the instant invention. Instant claims such as claim 334 are included as rejected hereinunder due to the above noted unclarity regarding the word "derived".

This application is a continuation under 37 CFR § 1.60. Therefore references made of record in prior parent applications are hereby also made of record as having been considered in the instant application. However, since this application has been filed under 37 CFR § 1.60 none of the PTO Form 1449s or 892s from prior parent applications are in the instant file. Applicants are therefore requested to supply copies of the executed 1449s and 892s from these parent applications so that they may be included for reference to citations in the instant file.

No claim is allowed.

Papers related to this application may be submitted to Group 1800 by facsimile transmission. Papers should be faxed to Group 1800 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 305-7401 or (703) 305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ardin Marschel, Ph.D., whose telephone number is (703) 308-3894. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, George Elliott, can be reached on (703) 308-4003.

Any inquiry of a general nature or relating to the status of this application should be directed to the Chemical Matrix receptionist whose telephone number is (703) 308-0196.

March 10, 1997

Ardin H. Marschel

ARDIN H. MARSCHEL
PRIMARY EXAMINER
GROUP 1800

The drawings filed (insert date) 01/17/06, are
A. ___ not objected to by the Draftsperson under 37 CFR 1.84 or 1.152.
B. X objected to by the Draftsperson under 37 CFR 1.84 or 1.152 as indicated below. The Examiner will require submission of new, corrected drawings when necessary. Corrected drawings must be submitted according to the instructions on the back of this Notice.

1. DRAWINGS. 37 CFR 1.84(a): Acceptable categories of drawings: Black ink. Color.
   - ___ Not black solid lines. Fig(s)___
   - ___ Color drawings are not acceptable until petition is granted. Fig(s)___
2. PHOTOGRAPHS. 37 CFR 1.84(b)
   - ___ Photographs are not acceptable until petition is granted. Fig(s)___
   - ___ Photographs not properly mounted (must use brystol board or photographic double-weight paper). Fig(s)___
   - ___ Poor quality (half-tone). Fig(s)___
3. GRAPHIC FORMS. 37 CFR 1.84 (d)
   - ___ Chemical or mathematical formula not labeled as separate figure. Fig(s)___
   - ___ Group of waveforms not presented as a single figure, using common vertical axis with time extending along horizontal axis. Fig(s)___
   - ___ Individuals waveform not identified with a separate letter designation adjacent to the vertical axis. Fig(s)___
4. TYPE OF PAPER. 37 CFR 1.84(c)
   - ___ Paper not flexible, strong, white, smooth, nonshiny, and durable. Sheet(s)___
   - X Erasures, alterations, overwritings, interlineations, cracks,creases, and folds copy machine marks not accepted. Fig(s) ALL
   - ___ Mylar, velum paper is not acceptable (too thin). Fig(s) ___
5. SIZE OF PAPER. 37 CFR 1.84(f): Acceptable sizes:
   - 21.6 cm. by 35.6 cm. (8 1/2 by 14 inches)
   - 21.6 cm. by 33.1 cm. (8 1/2 by 13 inches)
   - 21.6 cm. by 27.9 cm. (8 1/2 by 11 inches)
   - 21.0 cm. by 29.7 cm. (DIN size A4)
   - ___ All drawing sheets not the same size. Sheet(s)___
   - ___ Drawing sheet not an acceptable size. Sheet(s) ___
6. MARGINS. 37 CFR 1.84(g): Acceptable margins:

Paper size

	21.6 cm. X 35.6 cm. (8 1/2 X 14 inches)	21.6 cm. X 33.1 cm. (8 1/2 X 13 inches)	21.6 cm. X 27.9 cm. (8 1/2 X 11 inches)	21.0 cm. X 29.7 cm. (DIN Size A4)
T	5.1 cm. (2")	2.5 cm. (1")	2.5 cm. (1")	2.5cm.
L	.64 cm. (1/4")	.64 cm. (1/4")	.64 cm. (1/4")	2.5 cm.
R	.64 cm. (1/4")	.64 cm. (1/4")	.64 cm. (1/4")	1.5 cm.
B	.54 cm. (1/4")	.64 cm. (1/4")	.64 cm. (1/4")	1.0 cm.

Margins do not conform to chart above. Sheet(s)___ Fig 2
X Top (T) ___ Left (L) ___ Right (R) ___ Bottom (B)

7. VIEWS. 37 CFR 1.84(h)
   REMINDER: Specification may require revision to correspond to drawing changes.
   - ___ All views not grouped together. Fig(s)___
   - ___ Views connected by projection lines or lead lines. Fig(s)___

   Partial views. 37 CFR 1.84(h) 2
   - ___ View and enlarged view not labled separately or properly. Fig(s)___

   Sectional views. 37 CFR 1.84 (h) 3
   - ___ Hatching not indicated for sectional portions of an object. Fig(s)___
   - ___ Cross section not drawn same as view with parts in cross section with regularly spaced parallel oblique strokes. Fig(s)___
8. ARRANGEMENT OF VIEWS. 37 CFR 1.84(i)
   - ___ Words do not appear on a horizontal, left-to-right fashion when page is either upright or turned so that the top becomes the right side, except for graphs. Fig(s)___
9. SCALE. 37 CFR 1.84(k)
   - ___ Scale not large enough to show mechanism with crowding when drawing is reduced in size to two-thirds in reproduction. Fig(s)___
   - ___ Indication such as "actual size" or scale 1/2" not permitted. Fig(s)___
10. CHARACTER OF LINES, NUMBERS, & LETTERS. 37 CFR 1.84(l)
    - ___ Lines, numbers & letters not uniformly thick and well defined, clean, durable, and black (except for color drawings). Fig(s)___
11. SHADING. 37 CFR 1.84(m)
    - ___ Solid black shading areas not permitted. Fig(s)___
    - ___ Shade lines, pale, rough and blurred. Fig(s)___
12. NUMBERS, LETTERS, & REFERENCE CHARACTERS. 37 CFR 1.84(p)
    - ___ Numbers and reference characters not plain and legible. 37 CFR 1.84(p)(1) Fig(s)___
    - ___ Numbers and reference characters not oriented in same direction as the view. 37 CFR 1.84(p)(1) Fig(s)___
    - ___ English alphabet not used. 37 CFR 1.84(p)(2) Fig(s)___
    - ___ Numbers, letters, and reference characters do not measure at least .32 cm. (1/8 inch) in height. 37 CFR(p)(3) Fig(s)___
13. LEAD LINES. 37 CFR 1.84(q)
    - ___ Lead lines cross each other. Fig(s)___
    - ___ Lead lines missing. Fig(s)___
14. NUMBERING OF SHEETS OF DRAWINGS. 37 CFR 1.84(t)
    - ___ Sheets not numbered consecutively, and in Arabic numerals, beginning with number 1. Sheet(s)___
15. NUMBER OF VIEWS. 37 CFR 1.84(u)
    - ___ Views not numbered consecutively, and in Arabic numerals, beginning with number 1. Fig(s)___
    - ___ View numbers not preceded by the abbreviation Fig. Fig(s)___
16. CORRECTIONS. 37 CFR 1.84(w)
    - ___ Corrections not made from prior PTO-948. Fig(s)___
17. DESIGN DRAWING. 37 CFR 1.152
    - ___ Surface shading shown not appropriate. Fig(s)___
    - ___ Solid black shading not used for color contrast. Fig(s)___

COMMENTS: